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I also certify that the attached copy of the request for grant of a Patent (Form 1/77) bears an amendment, effected by this office, following a request by the applicant and agreed to by the Comptroller-General.

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Patents Form 1/77

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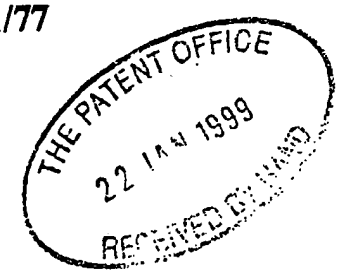

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D Young & Co

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P01/7700 0.00 - 9901479.7

Request for a grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office
Cardiff Road
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1. **Your reference** — P006203GB NJN

2. **Patent application number** *(The Patent Office will fill in this part)* — 22 JAN 1999 — **9901479.7**

3. **Full name, address and postcode of the or of each applicant** *(underline all surnames)*

COLLAG LIMITED,
MAIDENSTONE HEATH,
BLUNDELL LANE,
BURSLEDON,
SOUTHAMPTON,
SO31 1AA.

Patents ADP number *(if you know it)* 7005747001

If the applicant is a corporate body, give the country/state of its incorporation — BRITISH

4. **Title of the invention** — PROCESS FOR PRODUCING WATER SOLUBLE AND WATER DISPERSIBLE GRANULES

5. **Name of your agent** *(if you have one)* — D YOUNG & CO

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

21 NEW FETTER LANE
LONDON
EC4A 1DA

Wilbeck Greenall & Co
7 Stone Buildings
Lincoln's Inn
London
WC2A 3SZ

Patents ADP number *(if you have one)* — 59006 — 323001

6. **If you are declaring priority from one or more earlier patent applications, give the country and date of filing of the or each of these earlier applications and (if you know it) the or each application number**

Country	Priority application number *(if you know it)*	Date of filing *(day/month/year)*

7. **If this application is divided or otherwise derived from an earlier UK application, give the number and filing date of the earlier application**

Number of earlier application	Date of filing *(day/month/year)*

8. **Is a statement of inventorship and of right to grant of a patent required in support of this request?** *(Answer 'Yes' if:*
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
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YES

9. **Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document**

Continuation sheets of this form	–
Description	13
Claims(s)	–
Abstract	–
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10. **If you are also filing any of the following, state how many against each item.**

Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. **I/We request the grant of a patent on the basis of this application.**

Signature **Date**

D YOUNG & CO
Agents for the Applicants

22.01.1999

12. **Name and daytime telephone number of the person to contact in the United Kingdom**

NEIL NACHSHEN 0171 353 4343

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Notes

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PROCESS FOR PRODUCING

WATER SOLUBLE AND WATER DISPERSIBLE GRANULES

This invention relates to a process for the preparation of water dispersible and water soluble granules containing biologically active compounds and other substances. More particularly it relates to an extrusion process for the production of water dispersible granules of pesticides.

The advantages of dispersible granule formulations of pesticides are well known. Their ease of handling and reduced worker exposure compared to powder or liquid formulations are well documented. G. A. Bell, "Chemistry and Technology of Agrochemical Formulations", Edited by D. A. Knowles (Kluver, 1998), pages 80-114, describes a range of dispersible granule types and processes for their manufacture.

The most popular process for preparing dispersible granules is by extrusion. WO 89/00079 describes a process for the preparation of water dispersible granules which comprises mixing the desired ingredients of the granules to form an extrudable wet mix, which has a dough-like consistency, that is, a consistency analogous to a stiff dough produced in the bread making process. Such dough-like consistency may be provided by thorough mixing or kneading using a mixing apparatus such as a pug mill, double shafted auger, or an extrusion apparatus may

be adapted to provide suitable mixing. It also requires that after extrusion the wet extrusions are broken down by rolling, preferably in a tumbling action.

EP O 484 147 B1 describes a process for preparing dispersible propanil granules. The process comprises:

a) combining one or more surfactants with propanil and milling to a particle size of less than 20 microns to form a premix;

b) adding less than 25 percent by weight water and optionally a wetting agent to said premix and mixing until a paste is obtained;

c) granulating said paste thereby producing granules; and

d) drying said granules

Propanil is a relatively low melting point active prone to hydrolysis. It has been found that the formation of a paste is likely to cause degradation of the material during processing or on stability if the energy input during the paste formation is too high.

It has been found that the above described processes dictate a number of constraints on the desired ingredients of the granules. The energy input required in

the formation of the dough or paste can degrade certain low-melting, or temperature-sensitive, active materials. Water-soluble or slightly-soluble actives can form crystal bridges which inhibit the rapid and complete disintegration/dissolution of the granules on addition to water.

The handling of a dough or paste in a manufacturing plant can also cause problems with variation in viscosity due to temperature and/or shear conditions. This factor can lead to variation in product quality and yield. Finally, the rolling action required following extrusion can cause the formation of a "shell" of compacted material on the outside of the granule that leads to an increase in the drying time/temperature. There remains a need for improvements to existing known processes of preparing dispersible granules, that result in the production of granules with a high degree of suspensibility and dispersability as well as being a granular structure that is stable.

The present invention therefore relates to a method of preparing water dispersible granules comprising, the preparation of a pre-mix in the form of a free-flowing homogeneous powder comprising the active material together with suitable excipients, and extrusion of said powder in a low pressure extruder.

It has been surprisingly observed that water-dispersible and water-soluble granules can be produced using the above described process wherein the formation of a dough or paste is eliminated. The granules produced by such a process, exhibit improved characteristics on storage, dilution and in use.

The process involves the initial preparation of a pre-mix comprising the active material together with acceptable excipients in the form of a free-flowing homogeneous powder. Such a powder is preferably prepared by the adsorption of a liquid such as water, or any other suitable liquid onto a finely-divided active material, optionally mixed with acceptable excipients such as suitable surface-active agents (surfactants) such as dispersants and wetting agents, fillers, disintegrants, stabilisers, flow aids and the like. The premix is formed in a low-shear, high intensity blender such as a plowshare, ribbon, Y-cone, double cone or trough blender, so that a free-flowing, homogeneous powder is formed. If required the active material may be milled prior to the addition of the optional acceptable excipients or milled together with them.

The powder so formed is fed into a suitable low-pressure extruder, such as that described in EP 812256B, so that the premix is compacted against the apertures in the screen and forced through. The premix composition and extruder settings are such that the formation of a paste in the extruder is eliminated by virtue of

controlling the feeding and extruder blade speed thereby minimising agitation and excessive build-up of pre-mix in the hopper. The powder premix is converted into a compacted solid extrudate, which can be collected as a free-flowing granule in a suitable container.

As mentioned above an example of a suitable low pressure extruder is that described in EP 812256B, the content of which is hereby incorporated by reference, which eliminates the undesirable effect of the ingress of pastes which form as moist finely divided, water-insoluble powders are forced through the screen of conventional, low-pressure extruders.

Acceptable excipients that may be added to the active agent include ingredients, such as surface-active agents (surfactants) such as dispersants and wetting agents, fillers, disintegrants, stabilisers and flow-aids can be added prior to extrusion. The important factor in the choice of ingredient is the requirement that it does not cause any particle-to-particle interaction that may lead to the formation of a dough or paste during the process.

After the extrusion process, the granules so formed can be dried, if necessary, utilising a fluid-bed drier, tray dryer or other suitable equipment.

A final sieving step is carried out to remove under- and over-size material. Uniform, free-flowing granules are produced with excellent properties. Generally,

over 99% of the granules, prior to screening, are of a suitable size.

The elimination of the paste formation during the processing of the product, provides a wide choice of possible actives and ingredients, as any detrimental effects of the paste formation on the ingredients, and vice-versa, are no longer a factor. Ingredients can thus be chosen that produce the best properties in use, rather than the choice being compromised for processing issues.

The process is thus applicable to a wide range of active ingredients. Examples include but are not limited to a wide range of active ingredients. Examples include, but are not limited to pharmaceuticals, agricultural chemicals, oil field chemicals, animal feedstuffs and detergents.

The process is particularly suitable for, but not limited to, such agricultural chemicals as:

Abamectin, imidazolinone, ametryn, amitaz, atrazine, azoxystrobin, benomyl, bensulfuron-methyl, bentazone, bifenox, bromoxynil, captan, carbendazim, carfentrazone-ethyl, chloridazon, chlorothalonil, chlortoluron, chlorsulfuron, cinosulfuron, clodinafop, clopyralid, lambda-cyhalothrin, cyhexatin, cymoxynil, alpha-cypermethrin, deltamethrin, diflufenican, dimethomorph, diuron, ethofumesate, emamectin benzoate, fibronil, flurtamone, glyphosate, imazamethabenz-methyl, imazapyr, imazethapyr, imadacloprid,isoproturon,

linuron, mancozeb, maneb, metamitron, methiocarb, metribuzin, metsulfuron-methyl, milbectin, nicosulfuron, oxadixyl, oxyfluorfen, phenmedipham, pirimisulfuron-methyl, propanil, propyzamide, rimsulfuron, simazine, sulfometuron,-methyl, thifensulfuron-methyl, thiram, tribenuron-methyl, and triflusulfuron-methyl.

Suitable surface active agents may include either wetting or dispersing agents or a combination of both.

Examples of wetting agents include: sodium alkyl aryl sulphonates, sodium alkyl aryl sulphosuccinates, sodium alkyl sulphates.

Examples of dispersing agents include : sodium lignosulphonates, sodium naphthalene sulphonate formaldehyde condensates, tristyrylphenol ethoxylate phosphate esters, aliphatic alcohol ethoxylates, alkylphenol ethoxylates, EO-PO block copolymers, "comb" graft copolymers, polyvinyl alcohol-vinyl acetate copolymers.

Examples of disintegrants include : Bentonite, modified starch, polyvinyl pyrrolidone.

Examples of stabilisers include : citric acid, polyethylene glycol, BHT.

Examples of fillers include : starch, lactose, china clay, sucrose, kaolin.

In a particularly preferred embodiment, the active material is propanil that is air-milled together with disintegrants and flow agents prior to the addition of surfactants to form a mixture to which water is then adsorbed to form a a free-flowing homogeneous powder. The powder is then extruded using a low pressure extruder such as that described in EP 812 256B and the resultant granules dried.

The invention may be illustrated by the following examples but is in no way limited by them. A low-pressure extruder as described in EP 812,256B was used in each of the Examples below.

EXAMPLE I

Propanil 80 WG

The following formulation was prepared :

Propanil	80.0 %
Sodium alkyl aryl sulphonate	1.0 %
Sodium Lignosulphonate	10.0 %
Potato Starch	1.0 %
China Clay	to 100 %

The above formulation was prepared by first blending the Propanil Technical, China Clay and Starch in a plowshare blender for 5 minutes. The premix thus formed was then air milled to an average particle size of 5-7 microns. Water was added to the air milled pre-mix in a plowshare blender until a water content of approx. 18% was obtained. The free-flowing powder obtained was fed to a basket extruder of a design in which the formation of a paste was avoided. A compacted solid extrudate was obtained, which was dried at 65°C for 15 minutes until a moisture content of below 1.5% was obtained. The granules were tested as follows:

1 g of the granules were added to a measuring cylinder containing 100 mls of water. The

cylinder was inverted through 180 degrees and back again for one full inversion, taking 2 seconds and the number of seconds for complete disintegration observed. The cylinder was then allowed to stand for 30 minutes, undisturbed, and a 10 ml sample taken from the centre of the cylinder and analysed, gravimetrically, for the amount of solids present. This figure was then used to calculate the % of material in suspension after standing for this time. The results were compared to two commercial formulations of propanil, one (STAM® 80 EDF) manufactured by a standard extrusion technique involving the formation of a paste and the other (WHAM® 80DF) by pan granulation. The results obtained were as follows :

Commercial Product	Time Taken for Product to Disintegrate	% Remaining in Suspension after 30 minutes
Stam® 80 EDF	3-5 minutes	71.3
Collag Product	< 1 minute	86.9
Wham® 80 DF	> 5 minutes	9.9

The above results indicate the advantages of the product produced by the process described in this invention. In addition it was noted that the standard extruded product, Stam® 80EDF was badly caked in the commercial pack, indicating a physical degradation of the product on storage.

EXAMPLE 2

Chlorsulfuron 75 %

The following formulation was prepared:

Chlorsulfuron	75 %
Sodium alkyl aryl sulphonate	1%
Sodium lignosulphonate	12.5 %
China Clay	to 100 %

The above formulation was prepared by first blending the Chlorsulfuron Technical and China Clay in a plowshare blender for 5 minutes. The premix thus formed was then air milled to an average particle size of 3-4 microns. Water was added to the air milled pre-mix in a plowshare blender until a water content of approx. 14.5% was obtained. The free-flowing powder obtained was fed to a basket extruder of a design in which the formation of a paste was avoided. A compacted solid extrudate was obtained, which was dried at 60°C for 15 minutes until a moisture content of 0.9 % was obtained. The granules were tested as follows:

1 g of the granules were added to a measuring cylinder containing 100 mls of water. The cylinder was inverted through 180 degrees and back again for one full inversion, taking 2 seconds and the number of seconds for complete disintegration observed. The cylinder was then allowed to stand for 30 minutes, undisturbed, and a 10 ml sample taken from the

centre of the cylinder and analysed, gravimetrically, for the amount of solids present. This figure was then used to calculate the % of material in suspension after standing for this time. The results were compared to a commercial formulation of chlorsulfuron, (GLEAN® 75 DF) manufactured by a standard fl;uid bed agglomeration. The results obtained were as follows :

Commercial Product	Time Taken for Product to Disintegrate	% Remaining in Suspension after 30 minutes
Glean® 75 DF	< 1 minute	69
Collag Chlorosulfuron	< 1 minute	86

It was noted that the Glean® sample was much more dusty than the extruded sample produced by the process of the present invention. At the low use rate of the product, the higher supensibility of the product would lead to a higher availability in field use and a higher efficacy.

EXAMPLE 3

Chloridazon 65 DF

A commercial premix of Chloridazon 65 DF was obtained from which a commercial sample of water dispersible granule had been produced by a wet agglomeration technique.

The same premix was extruded using the process of the present invention and both samples were tested for suspensibility. The results obtained are as follows :

	% Suspensibility
Commercial Chloridazon 65 DF	89
Collag Extruded Chloridazon 65 DF	98